

A1 the patient, presents at least part of [said] the abnormal molecule, or molecule abnormally elevated, contained in or associated with the diseased cells of [said] the patient.

3. (Amended) A method according to Claim 1 [or 2] wherein the CTL are substantially free of other cell types.

Sub 2) 4. (Amended) A method according to [any one of Claims 1 to 3] Claim 1 wherein [said] the molecule is a polypeptide.

Sub 3) 5. (Amended) A method according to Claim 4 wherein [said] the polypeptide is a mutant polypeptide associated with [said] the diseased cells.

Sub 3) 6. (Amended) A method according to Claim 4 wherein [said] the polypeptide is present at a higher level in [said] the diseased cells compared to non-diseased cells.

Sub 4) 7. (Amended) A method according to [any one of the preceding claims] Claim 1 wherein the disease is a cancer.

Sub 5) 9. (Amended) A method according to [any one of Claims 1 to 6] Claim 1 wherein the disease is caused by a chronic viral infection.

Sub 6) 12. (Amended) A method according to [any one of Claims 1 to 6] Claim 1 wherein the disease is associated with an abnormally elevated amount of a hormone.

13. (Amended) A method according to [any one of Claims 1 to 6] Claim 1 wherein the disease is a bacterial disease caused by a chronic bacterial infection.

C4 14. (Amended) A method according to [any one of the preceding claims] Claim 1 further comprising the step of determining the HLA class I (or equivalent) molecule type of the patient prior to administration of the CTL.

15. (Amended) A method according to Claim 14 wherein the [said] type is determined using DNA typing.

16. (Amended) A method according to [any one of the preceding claims] Claim 1 wherein the patient is human.

Sub 7) 17. (Amended) A method according to Claim 14 wherein [said] the cytotoxic T lymphocyte is selected from a library of CTL clones, [said] the library comprising a

17. (Amended) A method according to Claim 16 wherein each [said] CTL clone recognises [said] the diseased cells.

18. (Amended) A method according to Claim 17 wherein each [said] CTL clone recognises at least part of the same molecule contained in or associated with [said] the diseased cells.

20. (Amended) A method of making a clonal population of cytotoxic T lymphocytes (CTL) reactive against a selected molecule the method comprising the step of (a) co-culturing a sample containing CTL or a precursor[,] thereof derived from a healthy individual with a stimulator cell which expresses HLA class I (or equivalent) molecules on its surface and that represents at least a part of the selected molecule in a large proportion of occupied [said] HLA class I (or equivalent) molecules present on the surface of [said] the stimulator cell and (b) selecting a CTL clone reactive against [said] the selected molecule when at least a part of [said] the molecule is presented by an HLA class I (or equivalent) molecule on the surface of a cell, wherein the healthy individual does not carry the HLA class I (or equivalent) molecule type which, on the stimulator cell, presents at least a part of the selected molecule.

21. (Amended) A method according to claim 20 wherein [said] the sample containing CTL or a precursor thereof is PBMC.

22. (Amended) A method according to Claim 20 wherein [said] the molecule is a polypeptide.

23. (Amended) A method according to [any one of Claims 20 to 22] Claim 20 wherein [said] the selected molecule is an abnormal molecule associated with a diseased cell, or a molecule associated with a diseased cell wherein an abnormally elevated amount of [said] the molecule is present in [said] the diseased cell.

24. (Amended) A method according to Claim 23 wherein the [said] selected molecule is a mutant polypeptide associated with a diseased cell or a polypeptide present at a higher level in [said] the diseased cell [compound] compared to a non-diseased cell.

25. (Amended) A method according to Claim 23 [or 24] wherein [said] the diseased cell is any one of a cancer cell, a virus-infected cell, a bacterium infected cell and a cell expressing an abnormally elevated amount of a hormone.

26. (Amended) A method according to [any one of Claims 20 to 25] Claim 20 wherein the healthy individual is a human.

27. (Amended) A method according to Claim 26 wherein the [said] selected molecule is any one of cyclin D1, cyclin E, mdm 2, EGF-R, erb-B2, erb-B3, FGF-R, insulin-like growth factor receptor, Met, myc, p53, BCL-2, ie mutant Ras, mutant p53, a polypeptide associated with the BCR/ABL translocation in CML and ALL[;], mutant CSF-1 receptor, mutant APC, mutant RET, mutant EGFR, a polypeptide associated with PML/RARA translocation in PML, a polypeptide associated with E2A-PBX1 translocation in pre B leukaemias and in childhood acute leukaemias, human papilloma virus proteins, Epstein-Barr virus proteins, HTLV-1 proteins, hepatitis B or C virus proteins, herpes-like virus proteins and HIV encoded proteins.

28. (Amended) A method according to [any one of Claims 20 to 27] Claim 20 further comprising determining the HLA Class I (or equivalent) type of the healthy individual.

29. (Amended) A method according to Claim 28 wherein [said] the HLA class I (or equivalent) type is determined by DNA analysis.

30. (Amended) A method according to [any one of Claims 20 to 29] Claim 20 wherein [said] the stimulator cell has a type of HLA class I (or equivalent) molecule on its surface which HLA class I (or equivalent) molecule type is not present in the healthy individual.

31. (Amended) A method according to [any one of Claims 20 to 30] Claim 20 wherein [said] the stimulator cell is a cell which is substantially incapable of loading [said] the HLA class I (or equivalent) molecule with at least a part of [said] the selected molecule.

As 32. (Amended) A method according to Claim 31 wherein [said] the cell is a mammalian cell defective in the expression of a peptide transporter.

34. (Amended) A method according to Claim 31 wherein [said] the cell is an insect cell.

35. (Amended) A method according to Claim 34 wherein [said] the cell is a *Drosophila* cell.

36. (Amended) A method according to [any one of Claims 20 to 35] Claim 20 wherein the stimulator cell is a host cell transfected with a nucleic acid molecule capable of expressing [said] the HLA class I (or equivalent) molecule.

37. (Amended) A method according to Claim 36 wherein [said] the host cell before transfection expresses substantially no HLA class I (or equivalent) molecules.

38. (Amended) A method according to [any one of Claims 20 to 37] Claim 20 wherein [said] the stimulator cell expresses a molecule important for T cell costimulation.

40. (Amended) A method according to [any one of Claims 20 to 39] Claim 20 wherein substantially all [said] the HLA class I (or equivalent) molecules expressed on the surface of [said] the stimulator cell are of the same type.

41. (Amended) A clonal population of cytotoxic T lymphocytes reactive against a selected molecule obtainable by the method of [any one of Claims 20 to 40] Claim 20.

45. (Amended) A library of CTL clones, [said] the library comprising a plurality of CTL clones derived from individuals and each [said] CTL clone is restricted by a different HLA class I allele and recognises a molecule associated with a selected disease.

47. (Amended) A method of making a cytotoxic T lymphocyte (CTL) suitable for treating a patient, the method comprising making a clonal population of CTL by the method of [any one of Claims 20 to 40] Claim 20; preparing a genetic construct capable of expressing the T-cell receptor (TCR) of the [said] clonal population of CTL, or a functionally equivalent molecule; and introducing [said] the genetic construct into a CTL or precursor thereof which CTL or precursor is derived from [said] the patient.

49. (Amended) A method of treating a patient with a disease wherein the patient contains diseased cells which cells contain, or are associated with, an abnormal molecule or an abnormally elevated amount of a molecule and which cells are capable of presenting at least part of [said] the molecule on their surface by an HLA class I (or equivalent) molecule, the method comprising administering to the patient a therapeutically effective amount of cytotoxic T lymphocytes (CTL) which recognise at least part of [said] the molecule when presented by an HLA class I (or equivalent) molecule on the surface of a cell wherein the CTL is a CTL according to Claim 48.

Remarks

Claims 1-18, 20-43, and 45-49 are pending. Claims 1, 3-7, 9, 12-18, 20-32, 34-38, 40, 41, 45, 47, and 49 have been amended. Claims 19, 44, and 50 have been canceled. In general, the claims have been amended to eliminate multiple claim dependencies and correct minor informalities. A copy of all of the pending claims as they are believed to have been amended is attached to this Amendment as an appendix. Pursuant to MPEP § 607, the filing fee for the application has been calculated based on the claims remaining in the application following this Amendment.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: 10 July 1998

ARNALL GOLDEN & GREGORY LLP
2800 One Atlantic Center
1201 West Peachtree Street
Atlanta, Georgia 30309-3450
(404) 873-8794
(404) 873-8795 (fax)